Remarks

After amendment, claims 1-2, 5-16 and 46-47 remain pending in the present application. No claims are canceled in this amendment. Claims 3 and 4 were previously cancelled as were claims 17-45. The amendment to the claims has been made to clarify the originally filed claims and to expedite allowance of the instant application. The amendment to the claims has been made to clarify the language of claims 1 and 12 and to address the Examiner's 35 U.S.C. §112, second paragraph rejection. Support for the amendment to the claims is found throughout the originally filed application and claims and in particular, original claim 13 (as applied to the amendment to claim 12). No new matter has been added by way of this amendment.

The Examiner has objected to or rejected previously pending claims 6 variously under 35 U.S.C. §112, first and second paragraphs and §102(b). For the reasons which are set forth in detail herein, in the sections which follow, as well as the attached declaration of inventor Dr. Laurence A. Cole, the presently pending claims are now in condition for allowance.

The Claim of Priority of the Present Application

The Examiner has objected to Applicants' claim of priority to provisional application no. 60/418,128, filed October 10, 2002, as that priority claim relates to certain pending claims in the present application, for the reasons which are stated in the office action on pages 2-3. This issue is relevant as it relates to the putative prior art cited by the Examiner against the instant application under 35 U.S.C.§102(a). Inasmuch as the cited prior art is a reference by the inventor of the present application, Applicant respectfully traverses the Examiner's rejection and in order to obviate this rejection and advance prosecution of the present application, Applicant encloses his declaration which clearly shows that Khanlian, et al., *American J. of Obstetrics and Gynecology,* May, 2003, 188:1254-9 ("Khanlian, et al.") is not prior art to the instant application because Applicant is a co-author of that paper and was solely responsible for any invention

disclosed in that reference (See M.P.E.P. §715.01(c)). Consequently, because Khanlian, et al. is not prior art[1] to the present invention, further discussion of this issue as it relates to the rejection of the claims based on Khanlian, et al. is rendered moot. Applicant also discusses this issue in his attached declaration and in the section which appears hereinbelow.

The Rejection of Claims 13-16 under 35 U.S.C. §112, Second Paragraph

The Examiner rejected previously pending claims 13-16 for the reasons which are presented in the office action on pages 3 and 4. Applicant has amended claims 12 and 13 to obviate any issues associated with this rejection. Applicant respectfully submits that claims 13-16 are now in compliance with 35 U.S.C. §112, second paragraph.

The Rejection of Claims 12, 5-16, 46 and 47 under 35 U.S.C. §112, First Paragraph

The Examiner has rejected previously pending claims 12, 5-16, 46 and 47 under 35 U.S.C. §112, First Paragraph for the reasons which are set forth in the office action at paragraph 5, on pages 2-6. The Examiner contends *inter alia* that the claims are non-enabled essentially because a determination of total hCG in a sample requires undue experimentation of the use of "in-house" assays to measure serum and urine samples and because the measurement of ITA as hyperglycosylated hCG is non-enabled and that the claimed amount of hCG cannot be measured pursuant to the present invention. Applicant respectfully traverses the Examiner's rejection.

It is respectfully submitted that the claimed invention is enabled. The invention as claimed relates to a method for measuring the total amount of intact hCG and ITA or

1 Applicant also contends that Khanlian, et al. is not prior art because Khanlain, et al. was published *after* the filing of the priority provisional application s.n. 60/418,128, filed October 10, 2002. A reading of the priority application evidences support for the instant invention. Notwithstanding that support, Applicant provides the enclosed declaration to obviate this issue (See M.P.E.P. §715.01(c) and to expedite the allowance of the instant application, rather than delay allowance to dispose of issues which have been mooted by the enclosed Cole declaration. In addition, Applicant has not seen the need to argue that the instant application is nonetheless patentable over Khanlian, et al. for reasons related to deficiencies (in relationship to the present invention) of that reference.

the total amount of intact hCG and ITA plus the free beta form of hCG in a biological sample from a patient at risk for gestational trophoblastic disease or quiescent gestational trophoblastic disease as claimed and determining the amount of total intact hCG plus ITA or total hCG plus beta core plus ITA with the amount of ITA measured *using an immunoassay which determines the selective binding of monoclonal B152 to ITA* in the sample such that a diagnosis of gestational trophoblastic disease or quiescent gestational trophoblastic disease may be made. It is respectfully submitted that the present invention is enabled.

The measurement of the amount of intact hCG,, ITA and beta core hCG as defined in the specification in a urine, serum or plasma sample is well known in the art. The approach to measuring this amount may be through an immunoassay, or other commercially available hCG tests. Indeed many commercial assays measure same. This is discussed in significant detail in the specification *inter alia,* at page 7, fourth full paragraph of the specification, as well as on pages 8-10. Approaches for measuring hCG in biological samples have been known for years and are well documented and routine in the art. The measurement of ITA as defined in the specification (containing both N-glycosyl linkages and O-glycosyl linkages as indicated in the specification) is also well known in the art. Analysis can be performed by any number of techniques as described in the present application at pages 8-10 and in particular, in an immunoassay using the B152 antibody which is specific for ITA (and the O-glycosyl linkages of ITA as previously explained in the Valmu, et al. paper and the previously enclosed paper of Birken). The ITA in the sample which is measured is that amount which is determined by binding to the B152 antibody. Indeed, B152 antibody is specific for ITA or hyperglycosylated hCG as that term is used in the present invention and as that hyperglycosylated form is measured pursuant to the present invention. The specific monoclonal antibody B152 which is set forth in the claims is specific for binding to ITA, ITA is the hyperglycosylated form of hCG which is measured in the present invention. The measurement of ITA is clearly enabled inasmuch as monoclonal antibody B152 measures the chemical species which Applicant has identified as ITA. That aspect of the invention is clearly enabled.

Thus, the present invention provides all of the well-known methods for measuring amounts of intact hCG, beta hCG and ITA in urine, serum and plasma samples from a patient. The remaining steps are also well-known and are enabled. It is respectfully submitted that the instant claims are clearly enabled.

Moreover, the Examiner is requested to review the enclosed declaration of Dr. Laurence A. Cole, Professor, University of New Mexico, Albuquerque New Mexico. His declaration clearly evidences the fact that the claimed invention is enabled inasmuch as the measurement of total hCG in a sample is rather facile, can be accomplished using a number of commercial or readily-available assays which existed at the time of the filing of the present application and otherwise could be accomplished using a number of techniques and approaches which were described in the original application and are readily applied without having the person of ordinary skill (i.e., a laboratory technician with relevant scientific training) engage in undue experimentation to make those measurements.

It is respectfully submitted that with the amendment to the claims and as supported by the accompanying Cole declaration, practicing the invention as claimed is clearly enabled. Indeed, contrary to the Examiner's view, practice of the present invention is not only not *undue,* it is rather facile. Note that the ITA measured is that which binds to monoclonal antibody B152, as already explained and as further supported by the attached Cole declaration. The measurement of intact hCG and beta hCG (generally, only a small percentage- <1% of any sample) is well known in the art. The measurement of ITA using monoclonal antibody B152 clearly is enabled. It is therefore respectfully submitted that the measurement of hCG, beta hCG and ITA as claimed in the biological sample is enabled, inasmuch as measurement of hCG, beta hCG and ITA in urine, plasma or serum is relatively facile and diagnosing the conditions as claimed flows directly and readily from those measurements. Inasmuch as the measurement of each of hCG, beta hCG and ITA as claimed is enabled, practicing the remaining steps of the claimed invention to determine the existence of the condition is also enabled and facile.

The method now clearly reflects the fact that the condition is detecting the presence or absence of invasive trophoblast cells in a patient, not the sample.

Regarding the argument that the claimed method is not enabled, Applicant notes that the amount of intact hCG and optionally, beta hCG as claimed may be measured using any number of methods which are available in the art and are well described in the literature. In addition, as noted, commercial immunoassays may also be utilized to measure hCG and beta hCG and may be preferably used (see the attached Cole declaration). These may be used directly or adapted with minor variation in order to obtain an amount of hCG in a sample. Antibodies are readily available commercially which may measure intact hCG and ITA, and optionally, beta hCG. Regarding the measurement of ITA, the preferred method for measuring ITA in a sample is through the use of monoclonal B152, which is readily available and is claimed. Thus, all of the components for practicing the invention are available and well known in the art, all of the steps are well known and practicing the method which simply relies on well known steps already known in the art using components which are readily available in the art evidences that the claimed method is clearly enabled. It is thus respectfully submitted that the presently pending claims are enabled. The Cole declaration further evidence compliance of the present invention with the first paragraph of 35 U.S.C. §112.

Given the detailed discussion of practicing the invention in the present application, the availability of components which could/can be used to practice the present invention and the supporting declaration of Professor Cole, Applicant respectfully submits that the instant claims are in compliance with the requirement of 35 U.S.C. §112, First Paragraph. Applicant respectfully requests the Examiner to withdraw his rejection on these grounds.

The Rejection of Claims 1, 2, 5, 6-16 and 47 under 35 U.S.C.§102(a)

The Examiner has rejected claims previously pending claims 1, 2, 5, 6-16 and 47 under 35 U.S.C. §102(a) as being anticipated by Khanlian, et al., *American J. of*

Obstetrics and Gynecology, May, 2003 188:1254-9 (Khanlian, et al.). Applicant respectfully traverses the Examiner's rejection and in order to obviate this rejection and advance prosecution of the present application, Applicant encloses his declaration which clearly shows that Khanlian, et al. is not prior art to the instant application because Applicant is a co-author of that paper and was solely responsible for any invention disclosed in that reference (See MPEP §715.01(c)). In particular, Ms. Sarah A. Khanlian, co-author of Khanlian, et al., was a technician working in Applicant's research laboratory under his guidance and supervision, and did not contribute to any invention which was disclosed in the cited reference. Likewise, a second co-author, Dr. Harriet O. Smith, a medical doctor, was a clinician working in the clinic which provided samples to Ms. Khanlian to run in experiments designed by Professor Cole. Although both Ms. Khanlian and Dr. Smith were extremely helpful to the project and consequently named as coauthors of the paper for their contributions, neither of them contributed to the claimed invention. Consequently, because Khanlian, et al. is not prior art to the present invention, the rejection of the claims is rendered moot. Applicant respectfully requests that the Examiner withdraw his rejection of the present invention based upon Khanlian, et al.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

Applicants have neither canceled nor added any claim. No fee is therefore due for the presentation of this amendment. No fee is due for the presentation of this response. If any fee is due or any overpayment has been made, please charge/credit Deposit Account No. 04-0838.

Should the Examiner wish to discuss the present application in an effort to advance its prosecution, the undersigned attorney may be reached at the telephone number set forth hereinbelow.

Respectfully submitted,

COLEMAN SUDOL SAPONE, P.C.

By: _____
Henry D. Coleman
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Dated: January 4, 2010
Enclosure (Cole Declaration)

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Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on January 4, 2010. HPC

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Henry D. Coleman